In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-1474V
Filed: April 28, 2023
PUBLISHED

LUCITA SINGLETON, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Horner Influenza ("Flu") vaccine; subclinical seizures; epilepsy; significant aggravation.

Renee J. Gentry, Vaccine Injury Clinic, George Washington University Law School Washington, DC, for petitioner.
Zoe Wade, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

On October 10, 2017, Lucita Singleton ("petitioner") filed a petition for compensation under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10-34 (2018).[2] (ECF No. 1.) Petitioner alleges that the influenza ("flu") vaccination that she received on October 21, 2014, caused her subclinical seizures and epilepsy. *Id.* For the reasons set forth below I conclude that petitioner is not entitled to an award of compensation.

[1] Because this decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the decision will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] All references to "§ 300aa" below refer to the relevant section of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period also specified in the Table. If so, causation is presumed and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In these cases, the presumptions available under the Vaccine Injury Table are inoperative. Instead, the petitioner bears the burden of showing by preponderant evidence that the vaccine recipient's injury was actually caused by the alleged vaccination, often referred to as "causation-in-fact". § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii); *see also Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

To show actual causation, petitioner must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1279; *Hines*, 940 F.2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination caused the alleged injury. *Althen*, 418 F.3d at 1279. The petitioner need not show that the vaccination was the sole cause of the injury or condition, but must demonstrate that the vaccination was a "substantial factor" and a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). This standard has been interpreted to require "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F.3d at 1278; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

In what has become the predominant framing of this burden of proof, the *Althen* court described the "causation-in-fact" standard, as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of the evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. That expert's opinion must be "sound and reliable." *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). The *Althen* court also indicated, however, that a Program fact finder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Althen,* 418 F.3d at 1280.

A petitioner may also allege that a vaccine caused a "significant aggravation" of a pre-existing condition. The Vaccine Act defines a significant aggravation as any change for the worse in a pre-existing condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health. § 300aa-33(4). Where a petitioner in an off-Table case is seeking to prove that a vaccination aggravated a pre-existing injury, petitioners must also establish three *additional* factors. *See Loving v. Sec'y of Health & Human Servs.*, 86 Fed. Cl. 135, 144 (Fed. Cl. 2009) (combining the first three *Whitecotton* factors for claims regarding aggravation of a Table injury with the three *Althen* factors for off table injury claims to create a six-part test for off-Table aggravation claims); *see also W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1357 (Fed. Cir. 2013) (applying the six-part *Loving* test.). The additional *Loving* factors require petitioners to demonstrate aggravation by showing: (1) the vaccinee's condition prior to the administration of the vaccine, (2) the vaccinee's current condition, and (3) whether the vaccinee's current condition constitutes a "significant aggravation" of the condition prior to the vaccination. *W.C.*, 704 F.3d at 1357.

II. Issues to be Decided

In this case, petitioner initially alleged in her petition that her flu vaccine caused her to suffer subclinical seizures and epilepsy. (ECF No. 1.) After the exchange of expert opinions, petitioner refined her contentions in her prehearing brief. She contends that she "was vascularly compromised prior to her influenza vaccination and, as such, must demonstrate significant aggravation" under the six-part *Loving* test. (ECF No. 56, p. 10.) Specifically, petitioner characterizes her burden as follows:

> (1) She must demonstrate that she had preexisting asymptomatic microvascular angiopathy (2) that ultimately evolved into Epilepsy (3) which is clearly a significant aggravation of her preexisting condition under the *Loving/Sharpe* criteria. Then she must show (4) a medical theory causally connecting the influenza vaccine with microvascular angiopathy, that theory must be reputable and based on reliable science, (5) a logical sequence of cause and effect between the influenza vaccine and her symptoms, that is, that her clinical picture fits the theory proposed, and (6) an appropriate temporal relationship between the influenza vaccine and the onset of her symptoms. In totality, Ms. Singleton needs to make a showing of these six prongs by a simple preponderance of the evidence, however the 4th *Loving* prong, i.e., the 1st *Althen* prong, need only be demonstrated to be biologically plausible.

(*Id*. at 11.)

For his part, respondent initially addresses this case in the context of the three-part *Althen* test, but also filed a reply addressing petitioner's contentions under the *Loving* test. (ECF Nos. 60, 61.) He contests petitioner's characterization of the burden of proof under *Althen* prong one. (ECF No. 60.) Respondent also asserts that, assuming *arguendo* petitioner had met her *prima facie* burden of proof, then petitioner's epilepsy would still be more likely to have been caused by a factor unrelated to vaccination, namely a viral infection diagnosed shortly after vaccination. (*Id*. at 25-26.)

In the interest of completeness, the analysis below will address the full six-part *Loving* test advocated by petitioner, though the analysis conducted pursuant to the overlapping *Loving* and *Althen* prongs (*i.e*., *Loving* prongs four through six/*Althen* prongs one through three) is substantially the same and dispositive under either type of analysis. Because petitioner has not met her burden of proof, it is not necessary to determine whether respondent has demonstrated petitioner's diagnosed viral syndrome as an alternative cause of her condition.

III. Procedural History

This case was originally assigned to Special Master Millman on October 10, 2017. (ECF No. 4.) Following an initial order issued on October 19, 2017, petitioner filed a series of medical records on October 25, and a statement of completion on November 29, 2017. (ECF Nos. 6-9.) Respondent subsequently filed his Rule 4(c) report recommending against compensation on August 7, 2018. (ECF No. 16.) In response, petitioner filed an expert report from Dr. Carlo Tornatore on January 22, 2019, and the accompanying medical literature on March 28, 2019. (ECF Nos. 20, 24.) On June 4, 2019, this case was reassigned to my docket. (ECF No. 27.)

Respondent filed a responsive expert report and medical literature from Dr. M. Steven Evans on August 16, 2019. (ECF No. 34.) Petitioner then filed a supplemental report from Dr. Tornatore on March 2, 2020. (ECF No. 41.) On April 7, 2020,

respondent filed his own supplemental expert report from Dr. Evans. (ECF No. 42.) On April 8, 2020, the parties filed a joint status report indicating that they believed this case was ripe for an entitlement hearing. (ECF No. 43.) On October 20, 2020, a two-day entitlement hearing was scheduled to commence on June 21, 2022. (ECF No. 45.) In the interim, petitioner filed additional medical records, medical literature, and an affidavit describing her condition. (ECF Nos. 46-49, 53, 57.) A prehearing order setting a briefing schedule and close of the record was issued on April 5, 2022. (ECF No. 50.) The parties filed their prehearing briefs on May 31, 2022. (ECF Nos. 56, 60.) Respondent filed a reply brief on June 7, 2022. (ECF No. 61.) A two-day entitlement hearing was held on June 21, 2022. (*See* ECF No. 65, Transcript of Proceedings ("Tr"), filed 07/07/2022.) Respondent filed additional medical literature on June 22, 2022. (ECF No. 63; Ex. FF.) On July 7, 2022, petitioner filed a status report confirming she "d[id] not wish to file a written response to Respondent's exhibit FF." (ECF No. 66.) This case is now ripe for a decision on entitlement.

IV. Factual History

a. As reflected in the medical records

Prior to her vaccination, petitioner showed no signs or symptoms of central nervous system disorder or neurologic or cognitive dysfunction. (*See* Ex. 4, p. 3 (noting no neurologic symptoms).) Petitioner's earliest record from February 17, 2012, documents a history of hypertension, anemia, and seasonal allergies. (*Id.*; Ex. 11, pp. 2-4, 33-34.) Based on her medical records, it appears that petitioner's upper respiratory symptoms were primarily the result of environmental allergies and only occasionally a viral infection. (Ex. 11, pp. 2-5, 33.) In addition to these physical health issues, petitioner also suffered from mild depression triggered by the passing of her sister and cousin (as evidenced in her mental health assessments). (Ex. 5, pp. 2-13.) On September 18, 2014, petitioner presented for a psychotherapy session wherein she reported an instance of crying at work and also described "cloudy thoughts" and "not being able to get it together." (*Id.* at 23.)

Petitioner received the flu vaccination at issue in this case on October 21, 2014. (Ex. 1, p. 1.) On October 27, 2014, she reported to the Community Clinic of Shelbyville & Bedford County ("Community Clinic") for an examination. (Ex. 6, p. 2.) During this visit, petitioner reported that she received the flu shot "at 2:30 [and] got sick at 5:30 . . . ." (*Id.*) Petitioner reported that she lost her appetite, could not think, had no energy, and had been sleeping a lot. (*Id.*) Petitioner's symptoms had reportedly lasted for six days and were becoming progressively worse. (*Id.*) She reported that she received a flu shot the year prior with no problems. (*Id.*) She was diagnosed with a viral syndrome "with complications," and treated with Biaxin, ibuprofen, fluids, and rest. (*Id.*)

Petitioner had a follow up for her viral syndrome on November 3, 2014, where she reported feeling better but noted that her appetite had not returned and that her energy level remained low. (Ex. 6, p. 4.) Augmentin and "flu vaccine?" were listed under allergies. (*Id.*) On November 17, 2014, petitioner returned for further follow up

on her condition and reported that she felt "much better" and was ready to resume working. (*Id.* at 3.) Petitioner continued to report memory issues and fatigue. (*Id.*) She was diagnosed with viral syndrome and recommended continued fluids and rest when needed. (*Id.*) Petitioner was seen again for further therapy and counseling of her depression on November 24, 2014, where she reported that after she received the flu vaccine she felt "so bad [she] thought [she] was going to die at one point." (Ex. 5, p. 25.)

More than six months later, on June 27, 2015, petitioner reported to Saint Thomas health for dental, blood pressure medication, and vision issues. (Ex. 7, p.2.) Petitioner's review of symptoms included fever and memory loss. (*Id*. at 3.) Petitioner was also seen for complaints of "memory impairment" at Saint Louise clinic by Social Worker Tiffany Thomas, Nurse Practitioner Cassandra Gladkowski, and Dr. Jessica Thomas. (Ex. 9, pp. 1-4.) Petitioner's medications included hydrochlorothiazide, iron, and metoprolol. (*Id.* at 1.) She reported that after receiving the flu shot in October of 2014, she did not "feel right" and developed fever and chills which worsened over several days. (*Id.* at 4.) Petitioner described "an explosion of colors," but denied any headaches. (*Id.*) She reported feeling "normal" approximately 3-4 months after her vaccination, though she still suffered from short term memory loss. Petitioner denied loss of memory of personal information, falling, and recent visual changes, but reported that she was "not as strong as [she] used to be." (*Id.*) On examination, she showed "no gross deficit of memory...but slightly abnormal neuro exam noted today." (Ex. 9, p. 5.) Petitioner had positive Romberg and nystagmus tests.[3] (*Id*.) Dr. Gladkowski did not feel a CT scan was necessary, but petitioner was referred to neurology with a history of "systemic symptoms with short term memory loss x 1 year." (*Id.*) Petitioner's labs showed elevated folate and glucose levels but were otherwise within normal ranges. (*Id.* at 10-12.)

Petitioner returned to Dr. Thomas on August 14, 2015, for a follow up on her memory problems. (Ex. 12, pp. 14–15.) Petitioner further explained her post-vaccine condition, noting that she received her vaccination on a Tuesday, and that by Thursday she would forget how she arrived at her place of employment. (*Id.* at 15.) She explained that she began "seeing expulsions [*sic*]" after taking Nyquil during the days after her vaccination and that at the time of this exam she had been experiencing episodes of hand spasms, described by Dr. Thomas as "draw[ing] up." (*Id.*) Petitioner did not report any gross deficits of memory or abnormal behavior like placing her keys in the freezer, but explained that she would forget to turn the water off and that she could not use the stove. (*Id.*) Petitioner's physical exam did not reveal any new issues. (*Id.*

[3] Romberg sign refers to "swaying of the body or falling when standing with the feet close together and the eyes closed; the result of loss of joint position sense, seen in tabes dorsalis and other diseases affecting the posterior columns." *Romberg sign,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=106448 (last accessed Mar. 6, 2023). A Nystagmus test, also called a Barany or caloric test, is conducted for ocular and vestibular functioning—"irrigation of the normal ear with warm water produces rotatory nystagmus (caloric nystagmus) toward the irrigated side; irrigation with cold water produces similar nystagmus away from that side." *Caloric test,* DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=112479 (last accessed Mar. 6, 2023).

at 16–17.) Dr. Thomas believed that petitioner may have experienced hypertensive urgency and "maybe [posterior reversible encephalopathy syndrome]," ("PRES"). (*Id.* at 17.) Dr. Thomas was concerned that petitioner "had a stroke or seizures that should now be treated." (Ex. 12, p. 17.) Dr. Thomas prescribed vitamin D, additional blood tests, an EEG, and a brain MRI. (*Id.*) Petitioner's brain MRI was conducted on August 20, 2015, revealing no restricted diffusion, "[v]ery mild periventricular increased flair signal," suggesting "minimal periventricular demyelinization [*sic*] likely from chronic small vessel [ischemic] disease, [and] chronic paranasal sinus changes." (*Id.* at 22.) Petitioner received her EEG on September 8, 2015, at Saint Thomas Rutherford Hospital. (Ex. 10, p. 9.) Her results showed abnormalities "due to right anterior temporal sharp waves concerning for an epileptogenic focus at this region," without any ictal discharges observed. (*Id.*)

On September 11, 2015, petitioner returned to Dr. Thomas who noted that petitioner's EEG showed "left temporal sharp[] waves." (Ex. 12, p. 10.) Dr. Thomas also suggested petitioner's memory loss "could be due to subclinical seizures," and prescribed a trial of Keppra. (*Id.*) Dr. Thomas wrote a letter noting that petitioner had a severe reaction to the flu vaccine and recommended against further flu immunization on October 23, 2015. (Ex. 11, p. 1.) On December 11, 2015, petitioner reported that Keppra had relieved her hand spasms and Dr. Thomas added amlodipine to petitioner's Keppra regimen. (Ex. 12, pp. 2-4.) At this point, Dr. Thomas assessed petitioner with unspecified convulsions. (*Id.* at 3.)

On February 18, 2016, petitioner was seen at the Community Clinic of Shelbyville & Bedford County. (Ex. 11, p. 16.) She reported increased weakness lowered blood pressure and was assessed with hypertension and "seizure disorder." (*Id.*)

Petitioner was seen by Dr. Thomas again on March 11, 2016. (Ex. 13, p. 1.) She reported that her right-hand spasms were returning, and that it felt "like how [it] gets with a seizure." (*Id.*) Petitioner also reported fatigue and depression "which she rates as a 9/10 (used to be 10/10)." (*Id.* at 1, 3.) Petitioner's physical exam did not reveal any new problems, and Dr. Thomas recommended switching from Keppra to oxcarbazepine ("OXC"). (*Id.* at 3.) Dr. Thomas assessed petitioner with "localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, without status epilepticus." (*Id.*)

Petitioner was seen by Dr. Paul Buechel at Saint Thomas on May 20, 2016, for a follow up on her memory issues. (Ex. 28, p. 32.) Petitioner reported that her memory had been poor ever since her flu vaccination in October of 2014. (*Id.*) She described not being able to remember bible verses as she did in the past and that she had difficulty cooking very familiar recipes. (*Id.*) Petitioner explained that she had never experienced an "actual seizure," but noted that "every 15 minutes, her hands tighten." (*Id.*) Petitioner also reported that Dr. Thomas had witnessed "both of her hands tightening and twisting at the same time," which led Dr. Thomas to the conclusion that petitioner was experiencing minor seizures. (*Id.*) However, because petitioner explained that she was "completely awake throughout these episodes," Dr. Buechel was

of the opinion that her hand spasms were "not at all likely seizures." (*Id.*) Dr. Buechel did however recommend that petitioner avoid further flu immunizations due to her reaction. (*Id.*)

Petitioner began psychiatric counseling at Centerstone Clinic on November 2, 2016. (Ex. 29, p. 9.) She reported anger, low motivation, low energy, stress, forgetfulness, and denied any depression, suicidal/homicidal ideations, or psychosis. (*Id.*) Petitioner further reported that she experienced an allergic reaction to the flu vaccine and developed epilepsy. (*Id*.) She also explained that she suffered from a stroke during the previous year. (*Id.*) Petitioner's intake summary noted that her presentation was consistent with a diagnosis of adjustment disorder, epilepsy, and hypertension, and was recommended individual therapy once to twice per month. (*Id.* at 10.)

Petitioner returned to Saint Thomas on September 1, 2017, and was seen by Dr. Rejane Lisboa with a chief complaint of seizures and memory problems. (Ex. 28, p. 28.) Petitioner reported the same history of present illness as she had to her previous care providers, adding that she suffered an episode "when [her] head and arms were moving" but had not experienced any seizure-type episodes since mid-late 2016. (*Id.* at 29.) She also reported that she believed her memory problems were becoming progressively worse, she described forgetting dates and where she placed objects, but that she had not had any trouble driving so long as she was not distracted. (*Id.* at 29-30.) Petitioner's exam was normal and Dr. Lisboa noted that early symptoms of Alzheimer's were not excluded. (*Id.* at 30.)

On May 22, 2018, petitioner underwent a two-day traumatic brain injury ("TBI") vocational assessment. (Ex. 24, p. 12.) The assessment noted petitioner experienced a prior back injury with minimal spondyltiic endplate degenerative changes at the C4, C5, and C6 levels with "mild degenerative changes in the vertebral endplates and facets with mild disc bulging causing a disc/osteophyte complex, cervicalgia, calcifying shoulder tendonitis, and left index finger bursitis." (*Id.* at 12–13.) Petitioner also reported memory impairments, inability to multi-task, difficulty sequencing, and decreased attention. (*Id.* at 13.) Petitioner's occupational therapist reported that petitioner suffered from "(1) decreased function use of right upper extremity; (2) decreased executive functioning; (3) decreased insight into viable vocational possibilities; [and] (4) transportation [problems]." (*Id.* at 14.) Petitioner's assessment team recommended a neuropsychological evaluation, hearing evaluation, extending the two-day assessment to four-days, and outpatient physical therapy if petitioner chose not to complete the extended assessment. (*Id.* at 16.) Petitioner returned for further TBI assessment on August 9, 2018. (Ex. 24, p. 18.) Of note, petitioner's cognitive testing showed that she was severely, moderately, or mildly impaired in all measures of memory function with her "recent memory" score being the lowest, at 43. (*Id.* at 22.)

Petitioner received a neuropsychological evaluation at Sabin Behavioral Health on December 20, 2018. (Ex. 23, p. 5.) She reported generally the same history as she had up to this point, with the addition of experiencing full-body tremors at some point

before the evaluation, though not specified. (*Id.*) She also explained that she had trouble remembering names, the things that people said, where she placed her personal belongings and had issues finding words, understanding directions, and maintaining focus. (*Id.*) Petitioner's memory indices were all observed to be "very low," with the exception of her visual working memory index, which was recorded as "low average." (*Id.* at 9.)

Petitioner was seen by physician's assistant John Kramer at Saint Thomas on October 18, 2019, for a follow up on her seizure disorder. (Ex. 28, p. 12.) Petitioner reported that her most recent seizure occurred seven months prior, and that her full-body tremors had returned. (*Id.* at 14.) PA Kramer noted that although petitioner carried a diagnosis of "localization-related epilepsy," this was "a working diagnosis," and asked petitioner to follow up with the hospital's epilepsy specialist. (*Id*. at 17.) He also noted that some of petitioner's symptoms were concerning for "functional neurological disorder," and classified petitioner's possible epilepsy as idiopathic and scheduled an EEG. (*Id.*) Petitioner's memory impairment was noted to be chronic, and the medical code lists "other amnesia." (*Id.*) Petitioner's EEG was conducted on December 4, 2019, and was interpreted as normal with "no evidence of focal or abnormal epileptiform discharges." (*Id.* at 38.)

Petitioner returned to Saint Thomas on April 8, 2020 and was seen by Dr. Vanderkolk for a follow up on her seizures and memory problems. (Ex. 28, p. 7.) Dr. Vanderkolk reviewed petitioner's medical history in detail, noting that her initial EEG was unavailable, and that petitioner's earlier brain MRI appeared normal with the ischemic changes typical for petitioner's age "and nothing apparently abnormal by my view." (*Id.* at 10.) Dr. Vanderkolk noted that, although the testing was limited due to being conducted via phone, petitioner's memory scores were quite poor. (*Id.*) Petitioner was also observed to have a short temper and sporadic thoughts. (*Id.*) Dr. Vanderkolk reviewed petitioner's December 2019 EEG, which "was within normal limits." (*Id.* at 11.) Dr. Vanderkolk also noted that petitioner was insistent on changing her medication, noting her "mood-related issues," though Dr. Vandkerkolk noted that Oxcarbazepine usually does not cause irritability or anger, and she wondered whether petitioner suffered an underlying psychiatric condition or bipolar disease. (*Id*. at 11.)

Petitioner's remaining medical records document routine requests for prescription refills or unrelated exams. (*See* Ex. 27, pp. 55-96.) On April 15, 2021, petitioner presented to nurse practitioner Shanna Gaither or a follow-up complaining of multiple side effects with her antiepileptic medications. (*Id.* at 73-75.) NP Gaither noted petitioner had not been seen by her neurologist in some time due to financial difficulties. (*Id.* at 74.) Petitioner denied any new complaints and was recommended to follow-up with her neurologist at St. Thomas or with a Vanderbilt neurologist. (*Id.* at 75.)

b. As reflected in Petitioner's Affidavit[4]

Petitioner filed an affidavit in support of her petitioner on February 7, 2022. (Ex. 25.) In her petition, petitioner affirms that she has never filed a civil action in relation to her vaccination or alleged vaccine reaction. She also affirms that she has experienced her symptoms for longer than six months and that she had no history of seizures, cognitive issues, or memory problems. She further affirms that she received the flu shot at her place of employment on October 21, 2014, that she received the shot "high on [her] arm" and that it was "very painful and burning." Petitioner also reports that she experienced swelling at the injection site and began to feel really cold and dizzy approximately three hours after receiving the vaccination. (*Id.* at 1.)

Petitioner then affirms that she took NyQuil and slept until 1:40 PM the following day. She struggled to make it in to work and continued to feel sick and cold. Petitioner also experienced hallucinations and felt dizzy and delirious. Petitioner states that she experienced a seizure lasting approximately two minutes at 7:00 PM where both of her hands seized and spasmed, but she did not report this to her supervisors for fear of being fired. (Ex. 25, p. 2.) The following day, petitioner was asked to operate a tow motor, but declined, explaining to her supervisor that she did not feel safe operating the machinery. Petitioner reported that she fell asleep during the drive home from work that day. (*Id.*) The second day after her vaccination, petitioner was let go from her job. She states that she was able to drive home but did not remember the drive to or from work. (*Id.*) Petitioner further affirms that she spent that weekend in bed, hardly able to get out and experiencing continued chills and significant swelling of her injection site. (*Id.*) She experienced "explosions in [her] head like fireworks" and "saw colors." Petitioner explains that she felt as though "cold air was pouring down" her brain through "a hole" in her head. (*Id.*)

Petitioner's symptoms led her to seek treatment at a free clinic on October 27, 2014. (Ex. 25, p. 2.) She was observed to have a fever of 101 degrees and flu was suspected. (*Id.*) Petitioner was discharged after receiving a negative flu test and told to seek help at the ER if she continued to feel ill. (*Id.*) Petitioner affirms that by October 27, 2014, she had a cough, fever, and chills all lasting for six days, but no sore throat. (*Id.*) Petitioner's symptoms slowly resolved in the subsequent weeks, but she continued to seek treatment after being referred to Dr. Thomas, a neurologist. (*Id.*) Petitioner affirms that Dr. Thomas diagnosed her with epilepsy which was believed to have been triggered by her reaction to the flu shot. (*Id.*) Dr. Thomas prescribed the anti-epileptic drug Keppra, which petitioner believed caused "horrible depression and suicidal thoughts," in addition to making her often angry, upset, and easily agitated. (*Id.*) Due to these side effects, Dr. Thomas ceased Keppra and prescribed Oxcarbazepine which petitioner indicated caused her to feel rage and experience homicidal thoughts without stopping her seizures. (*Id.*) Ultimately, petitioner was prescribed lamotrigine which she states has lessened the effects of her seizures. (*Id.* at 3.)

[4] Petitioner did not testify at the entitlement hearing held on June 21, 2022. (Tr. 4.)

Petitioner explains that she has had severe issues with her short-term memory and reading comprehension. (*Id*.) Petitioner concludes her affidavit by writing that she feels angry about her situation. (*Id*.) Specifically, she mentions being unable to able to work; being a burden on her family; failing to meet her financial obligations; and losing independence and community connection. (*Id.* at 3-4.)

V. Summary of Expert Opinions and Qualifications

a. Petitioners' Expert – Carlo Tornatore, M.D.

Dr. Tornatore provided two expert reports in this case and testified at the entitlement hearing. (Exs. 15, 22, Tr 5-202, 277-88.) He has been offered by petitioner without objection as an expert in neurology and neuroimmunology.[5] (Tr. 10-11.)

i. Expert reports

Dr. Tornatore opines petitioner had "no symptoms referable to the central nervous system" prior to her vaccination, and that she developed systemic neurological symptoms shortly thereafter. (Ex. 15, p. 5.) Dr. Tornatore opines that petitioner's neurologic symptoms, which were primarily cognitive symptoms, persisted and could be explained by the microvascular angiopathy/small vessel ischemic disease evidenced by her initial MRI. (*Id.* (citing Johann Selvarajah et al., *Potential Surrogate Markers of Cerebral Microvascular Angiopathy in Asymptomatic Subjects At Risk Of Stroke*, 19 EUR. RADIOLOGY 1011 (2009) (Ex. 17)).) Dr. Tornatore explains that small vessel ischemic disease "is a result of atherosclerotic narrowing of the small caliber vessels of the brain due to either hypertension, diabetes, or hyperlipidemia." (Ex. 15, p. 5.) He concedes that petitioner had hypertension, and thus, "clearly" had risk factors for cerebrovascular disease, but was never symptomatic prior to her vaccination. (*Id.*) Dr. Tornatore also opines that petitioner's cognitive symptoms are consistent with ischemic disease and that it is likely she had "significant aggravation of pre-existing risk factors," which were confirmed by petitioner's subsequent EEG testing showing sharp waves consistent with neuronal irritation. (*Id.* at 6.) According to Dr. Tornatore, the two most common causes of "EEG changes" in a patient over the age of 50 are ischemic disease and tumor. Petitioner's MRI showed no evidence of any malignancy, therefore Dr. Tornatore opines it is likely that petitioner suffered from ischemic disease. (*Id.*) Dr. Tornatore concludes that petitioner's symptoms did not arise until after her vaccination,

[5] Dr. Tornatore is currently Chair and Neurologist-in-Chief of the Georgetown University Hospital department of neurology and regional director for neurology at Medstar Health. He previously served as vice chair of Georgetown's department of neurology, and professor of neurology at Georgetown University Medical Center. (Ex. 26, p. 3.) Dr. Tornatore received his bachelor's degree in neurobiology at Cornell University and holds a master's degree in physiology and a medical degree from Georgetown University. (*Id.* at 2.) Dr. Tornatore completed his internship in internal medicine at Providence Hospital in Washington, DC and his residency in neurology at Georgetown University Hospital. (*Id.*) Dr. Tornatore is currently licensed to practice medicine in the District of Columbia and board certified in Neurology by the National Board of Psychiatry and Neurology. (*Id.* at 1.) He testified that he "also attend[s] on service…[and] [sees] stroke patients, so I'm very familiar with vascular disease of the nervous system as well as coronary artery disease, which is part and parcel with it." (Tr. 10.) Dr. Tornatore has published 58 different peer reviewed articles and five book chapters on neurology and virology. (Ex. 26, pp. 8–14.)

and therefore, there is a logical sequence of cause and effect suggesting that her vaccination triggered her ischemic disease which led to her neurologic symptoms. (*Id.*)

Dr. Tornatore opines it is biologically plausible that vaccination can cause or aggravate vascular disease / microvascular angiopathy. (*Id*.) According to Dr. Tornatore, it is "well recognized that vascular disease is caused by a cascade of inflammatory changes in the wall of blood vessels." (Ex. 15, p. 6.) He explains that atherosclerosis involves an ongoing inflammatory response. (*Id.* (citing Peter Libby et al., *Inflammation and Atherosclerosis*, 105 CIRCULATION 1135 (2002) (Ex. 18)).) Dr. Tornatore opines it "is well recognized that the influenza vaccination results in a variety of inflammatory responses." (Ex. 15, p. 6.) He cites a study finding a measurable acute phase response following influenza vaccination in men with and without severe carotid artery disease. (*Id.* (citing Cara L. Carty et al., *Inflammatory Response After Influenza Vaccination in Men With and Without Carotid Artery Disease*, 26 ARTERIOSCLER THROMBOSIS VASCULAR BIO. 2738 (2006) (Ex. 20)).) Based on these studies, Dr. Tornatore concludes that "a vaccine-induced inflammatory cascade" could result in vascular disease similar to what was seen on petitioner's MRI and EEG. (Ex. 15, pp. 6–7.)

Dr. Tornatore cites a case report of a 75-year-old man who developed a stroke after influenza/H1N1 vaccination. (Ex. 15, p. 7 (citing Yi-Pin Lin et al., *Ischaemic Stroke and Influenza A H1N1 Vaccination: A Case Report*, 2 ARCHIVES MED. SCI. 345 (2011) (Ex. 21)).) The authors noted that the VAERS data suggested that the seasonal flu vaccine was the most common vaccine associated with ischemic stroke, that ischemic stroke occurred within a day of vaccination in 18% of patients, and that flu vaccination may result in a pro-thrombotic state due to immune upregulation. (Ex. 15, p. 7.) Dr. Tornatore opines that this medical literature is relevant to petitioner's case because she "already had risk factors for atherosclerotic disease/narrowing of the small vessels," which could have been aggravated by a flu vaccination causing the cognitive issues and sharp waves seen on EEG. (*Id.*) Ultimately, Dr. Tornatore opines that petitioner's October 21, 2014, flu vaccination aggravated her pre-existing atherosclerotic disease causing the neuronal irritability and cognitive symptoms she alleges. (*Id.*)

In his supplemental report, Dr. Tornatore focuses primarily on what he considers points of agreement with Dr. Evans. (Ex. 22.) Dr. Tornatore summarizes his opinion as follows: "[petitioner] developed symptomatic microvascular disease of the central nervous system attributable to the influenza vaccination she received on October 21, 2014. (Id. at 2.) This [is] based on a striking temporal relationship between the onset of her symptoms, a logical sequence of cause and effect and a biologically plausible mechanism by which vaccination could cause aggravation of pre-exiting microvascular disease." (*Id*.) By Dr. Tornatore's account, the primary, if not only, point of disagreement between the experts is whether petitioner's pre-vaccination complaints of cognitive concerns during therapy are grief related (per Dr. Tornatore) or consistent with her later cognitive complaints (per Dr. Evans). (*Id*. at 3-4.) Dr. Tornatore suggests that Dr. Evans contradicts himself when he suggests that petitioner complained of cognitive issues prior to her vaccination, e.g., her complaints of "cloudy thoughts" and "not being

able to get it together," while also writing that they appeared to be related to her depression. (*Id*. at 3.)

ii. Testimony

Dr. Tornatore also testified during the hearing. (Tr. 5-203, 277-88.) He clarified that his opinion is "the influenza vaccination that [petitioner] received on October 21st, 2014, resulted in an inflammatory response that significantly aggravated her underlying microvascular angiopathy, resulting in a convulsive disorder and the symptomatically cognitive issues that were persistent." (*Id.* at 12.) Specifically, Dr. Tornatore opines that petitioner received the flu vaccine at issue, suffered "clear systemic symptoms related to the vaccine, which are chemokine- and cytokine-related that happen within a short period" causing endothelial changes or changes in blood vessel tone that mimic a wild-type influenza virus, "which we know can cause cerebrovascular disease." (*Id.* at 62.) In turn, "cerebrovascular disease is the most common…cause of epilepsy when you can identify a cause for it." (*Id.*)

Animal models, according to Dr. Tornatore, have demonstrated inflammatory responses to vaccination. (*Id.* at 42 (citing Jacqueline McDonald et al., *Inflammatory Responses to Influenza Vaccination at the Extremes of Age,* 151 IMMUNOL. 451 (2017) (Ex. 19)).) Dr. Tornatore referred to results from a mouse study that reported a positive correlation between an animal's inflammatory response and its age. (*Id*. (citing McDonald et al, *supra* at Ex. 19.).) Specifically, Dr. Tornatore pointed out that neonatal mice had more IL-1 alpha; young adult mice had more TNF alpha; and elderly mice had more IL-1 receptor agonist. (Tr. 42.) Dr. Tornatore asserted that the post-vaccine increase in inflammatory markers in mice is identical to an increase observed in humans. (*Id.* (citing Libby et al., *supra* at Ex. 18).)

Dr. Tornatore proposes that petitioner experienced a "cytokine response" post-vaccination, which reproduced "the exact same response that one gets with the wild-type infection." (Tr. 30.) He referred to two studies that support this theory. (*Id*. at 29-30.) The first study examined recipients of solid organ transplant and compared responses to vaccination versus natural infection. (Id. at 29 (citing Arnaud G. L'Huillier et al., *T-cell responses following Natural Influenza Infection or Vaccination in Solid Organ Transplant Recipients*, 10 SCI. RPT. 1 (2020) (Ex. 34)).) Dr. Tornatore acknowledged that petitioner did not have an organ transplant. (*Id.*) He nevertheless relies on the cytokine response observed in this study to infer that petitioner experienced a cytokine response to vaccination, which was of a similar amplitude to an expected response to wild-type infection. (*Id.* at 30.) The second study examined serum cytokines and chemokines after vaccination. (*Id.* (citing Kawsar Talaat et al., *Rapid Changes in Serum Cytokines and Chemokines in Response to Inactivated Influenza Vaccination,* 12 INFLUENZA OTHER RESPIR. VIRUSES 202 (2018) (Ex. 35)).) Dr. Tornatore highlighted an outlier in this study, who showed the most robust cytokine response: a 32-to-64-fold increase in hemagglutination-inhibition titer. (Tr. 31 (citing Talaat et al., *supra*, at Ex. 35).) Dr. Tornatore suggested this increase could be due to prior exposure to either to the virus or to a similar vaccine. (*Id*. at 32.) Regardless, he

stressed that this study demonstrates that patients may experience a significant cytokine and chemokine response within a short period of time, even within hours of vaccination – "as was the case with [petitioner]." (Tr. 32.)

Dr. Toratore opines, "whether you get an infection or whether you get vaccinated, the cytokine patterns are identical[,] [though] [t]he amplitude may be less noted." (*Id.* at 29-30.) Dr. Tornatore testified that the Nichols paper, cited by Dr. Evans, speaks to this same concept. (*Id.* at 55.) Dr. Tornatore testified "[p]ossible mechanisms of the increased risk of cerebrovascular and cardiovascular events after upper respiratory tract infection, such as influenza, include alterations in circulating clotting factors, platelet aggregation and lysis, concentration of inflammatory response proteins and alteration in cytokine concentrations." (*Id.* (quoting Kristin Nichols et al., *Influenza vaccination and reduction in hospitalizations for cardiac disease and stroke among the elderly,* 34 N. ENGL. J. MED. 1 (2003) (Ex. EE)).) These changes, according to Dr. Tornatore, "might enhance thrombotic tendencies, impair basal dilation, or cause endothelial injury." (Tr. 55.) To Dr. Tornatore, the evidence suggesting flu infection can cause an increased risk of cerebrovascular and cardiovascular events supports the theory that the flu vaccine can significantly aggravate thrombotic tendencies or endothelial injury in a vaccinee like petitioner who is predisposed to such cerebrovascular events. (*Id*. at 33.)

During the hearing Dr. Tornatore offered an additional case report by Thoon and Chan, describing a pediatric stroke case post influenza vaccination. (Tr. 46-7 (citing Koh Cheung Thoon & Derrick Wei Shih Chan, *Childhood stroke after influenza vaccination,* 21(2) PROC. SINGAPORE HEALTHCARE 296 (2012) (Ex. 31)).) The authors acknowledged that this was the first reported case, and Dr. Tornatore likewise opined that "[t]his is very unusual – you know, children don't get strokes." (Tr. 47 (citing Thoon & Chan, *supra*, at Ex. 31).) The ten-year-old developed a stroke in the cerebellum one day after receiving the seasonal trivalent influenza vaccine. (Tr. 47.) Dr. Tornatore acknowledges the possibility that the child may have been predisposed to stroke but maintained that "this may have been an inflammatory event that caused this stroke due to the vaccine, given the very striking temporal relationship and the…absolute rarity of stroke in children." (*Id*.) He stresses the usefulness of case reports in teaching the "clinical tempo" of disease, including rare diseases. (*Id*.) Among the case reports filed in this case, Dr. Tornatore underscores the fact that each had "the same kinetics of a stroke within a very short period of the vaccinations." (*Id.* at 48.)

b. Respondent's Expert – Steven Evans, M.D.

Dr. Evans likewise provided two reports and testified at the entitlement hearing. (Ex. A, CC, Tr. 203-277.) He has been offered by respondent without objection as an expert in neurology and epilepsy.[6] (Tr. 208.)

[6] Dr. Evans received his medical degree in 1982 and his Master of Science degree in physiology in 1984 from the University of Louisville. (Ex. B.) He completed his neurology residency training and chief residency at Barnes Hospital and the Washington University School of Medicine. (*Id.*) He completed a research fellowship in neuropharmacology at the same institution. (*Id.*) Dr. Evans currently serves as a practicing neurologist, partially retired, subspecializing in the diagnosis and treatment of epilepsy. (Ex. A, p. 1; Tr. 204.) He attends the epilepsy monitoring unit at the University of Louisville, where he sees

i. Expert reports

Dr. Evans opines that petitioner simply suffered from influenza or a flu-like syndrome after her vaccination which triggered her symptoms. (Ex. A, p. 4.) He writes that petitioner's complaints of "cloudy thoughts" and "not being able to get it together," were thought to be related to her depression and that her subsequent memory issues were never objectively observed on physical exam. (*Id.*) Dr. Evans concludes that isolated memory loss has not been reported as an adverse reaction to vaccination and characterizes her pre-vaccination complaints as similar to her memory complaints. (*Id.*)

With regard to petitioner's epilepsy diagnosis, he opines that her "neurological symptoms and results of testing point to a diagnosis of right temporal lobe epilepsy." (*Id.* at 4.) He explains that epilepsy is a condition that predisposes an individual to seizures, and that the condition precedes the seizures, but cannot be definitively diagnosed before seizures occur. (*Id.*) He further explains that seizures may be generalized or focal in onset and that seizures affecting or originating in the temporal lobe characteristically produce temporary amnesia in the ictal and postictal state, with occasional long-lasting temporary amnesia or other memory-related symptoms such as déjà vu or jamais vu. (Ex. A, p. 4 (citing Olivier Felician et al., *Transient epileptic amnesia: Update on a slowly emerging epileptic syndrome*, 171 REVUE NEUROLOGIQUE 289 (2015) (Ex. K)).)

Dr. Evans notes that temporal lobe epilepsy is usually associated with chronic memory loss and cognitive deficits specifically associated with memory. (Ex. A, p. 4 (citing Eve Tramoni-Negre et al., *Long-term memory deficits in temporal lobe epilepsy*, 173 REVUE NEUROLOGIQUE 490 (2017) (Ex. X); Cettina Allone et al., *Neuroimaging and cognitive functions in temporal lobe epilepsy: A review of the literature,* 381 J. OF NEUROLOGICAL SCI. 7 (2017) (Ex. C)).) Dr. Evans writes that the chronic memory loss of epilepsy "causes difficulty making new memories, not the forgetting of already-established memories . . ." (Ex. A, p. 4.) Further, "the memory complaint[s] of persons with epilepsy is chronic and bothersome, but nonprogressive," which also appears consistent with petitioner's symptoms. (*Id.*) According to Dr. Evans, the causes of memory dysfunction in temporal lobe epilepsy include brain tissue damage, seizures, medications, and associated mood disorders, especially depression. (*Id.* (citing Matthew J. Knight & Bernhard T. Baune, *Cognitive dysfunction in major depressive disorder*, 31 CURRENT OPINIONS IN PSYCHIATRY 26 (2017) (Ex. P)).)

Dr. Evans agrees that petitioner's EEG showing right temporal epileptiform discharges is an inter-seizure pattern highly suggestive of right temporal lobe epilepsy. (Ex. A, p. 5.) However, he writes, evidence of "small vessel ischemic disease on MRI is very common, and is associated with age, hypertension, and diabetes. Non-lesional temporal lobe epilepsy is very common, almost the rule rather than the exception. (*Id.* (citing Wolfgang Muhlhofer et al., *MRI-negative temporal lobe epilepsy–What do we*

patients and reads EEGs. (Tr. 204.) He also currently serves as a full Professor in the Department of Neurology at the University of Louisville. (Ex. A, p. 1.) He is board-certified in Neurology and also boarded in Clinical Neurophysiology and Epilepsy. (*Id.*)

know?, 58 EPILEPSIA 727 (2017) (Ex. U)).) Dr. Evans writes that additional confirmatory testing for epilepsy such as formal validation of bedside mental status, neuropsychological testing, and prolonged EEG monitoring was not done. (Ex. A, p. 5.)

Despite the above, Dr. Evans emphasizes that "no definite occurrence of seizures" were ever documented. (Ex. A, p. 5.) With regard to petitioner's hand spasms, he explains that spasms with retained consciousness are only very rarely seizures. (*Id.*) Further, Dr. Evans writes that focal onset epilepsy with focal motor seizures causes unilateral hand convulsions in the limb opposite to the epileptic brain tissue, while petitioner complained of bilateral spasms and later, right hand spasms and cramping. (*Id.*) Although Dr. Evans concedes that unilateral limb convulsions can occur in temporal lobe epilepsy, "the more prominent symptoms in this seizure type is sudden alteration of consciousness, and amnesia is the rule, so the convulsion symptoms must be reported by witnesses." (*Id.*) With no indication that any of petitioner's alleged seizures were witnessed by treating physicians or lay witnesses, Dr. Evans concludes that the characterization of her hand spasms as seizures is "very questionable." (*Id.*)

Moreover, petitioner's physicians believed that she suffered from subclinical seizures; and Dr. Evans notes that "[t]he concern was that non-convulsive or subtle seizures may have been occurring, and could be the cause of her complaint of memory loss." (Ex. A, p. 5.) He opines this condition is "relatively rare, and can only be substantiated by prolonged video-EEG monitoring and subsequent relief of seizures and symptoms by treatment with antiepileptic drugs." (*Id.*) Notably, in 30 to 50% of cases, symptoms thought to be the result of seizures were found to be psychogenic, non-epileptic events. (*Id.*) Dr. Evans emphasizes that "the effect of the therapeutic trial of Keppra on her memory was not specifically noted by clinicians." (*Id.*) As for petitioner's reported hallucination, Dr. Evans opines that this symptom "does not help to refine a neurological diagnosis," as "psychosis and seizures are symptoms of limbic encephalitides, especially anti-NMDA-receptor encephalitis [and] only one case report has appeared linking vaccination to anti-NMDA-receptor encephalitis . . . ." (*Id.* (citing L Hozakova et al., *Anti-NMDAR encephalitis as a serious adverse event probably related to yellow fever vaccination*, 24 CLIN. MICROBIO. INFECTION 17 (2018) (Ex. O)).) Thus, the link between these symptoms and vaccination must be considered "extremely tenuous." (Ex. A, p. 5.) In Dr. Evans opinion, petitioner's epilepsy diagnosis is "very reasonable," but because "no epileptic seizures were noted, the diagnosis would be provisional." (*Id*.)

Turning to the question of whether petitioner's vaccination could cause her epilepsy, Dr. Evans reports that he was unable to locate any cases of temporal lobe epilepsy following vaccination, but that seizures in epileptic patients are commonly precipitated by viral illness, bacterial infection, and fever. (*Id.* at 6.) Dr. Evans notes that petitioner complained of fever and was diagnosed with a viral syndrome shortly after her vaccination. (*Id.*) He explains that studies of pediatric patients have found that fever is associated with seizures even in those without epilepsy, and that while vaccinations have been found to slightly, or not at all, increase the risk of seizure in epileptic children, no association between epilepsy and vaccination has ever been

found.[7] (*Id.* (citing Lisen Arnheim-Dahlstrom et al., *Risk of presentation to hospital with epileptic seizures after vaccination with monovalent AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine (Pandemrix): self controlled case series study*, 345 BMJ e7594 (2012) (Ex. F); Inger Johanne Bakken et al., *Febrile seizures after 2009 influenza A (H1N1) vaccination and infection: a nationwide registry-based study*, 15 BMC INFECTIOUS DISEASES 506 (2015) (Ex. G); Xin Li et al., *The influence of vaccine on febrile seizure*, 16 CURRENT NEUROPHARMACOLOGY 59 (2018) (Ex. S); Karina A. Top et al., *Risk of seizures after immunization in children with epilepsy: a risk interval analysis*, 18 BMC PEDIATRICS 134 (2018) (Ex. W); Siri E. Haberg et al., *Epilepsy in children after pandemic influenza vaccination*, 141 PEDIATRICS e20170752 (2018) (Ex. M)).) Dr. Evans reports that he was unable to find any reported cases of temporal lobe epilepsy where the first seizures were precipitated by vaccination, but indicates that he has treated patients whose first seizures were precipitated by a viral illness. (Ex. A, p. 7.) Ultimately, Dr. Evans concludes that the medical records suggest that petitioner's epilepsy was triggered by a viral illness and not her vaccination. (*Id.*)

Finally, Dr. Evans addresses several claims made by Dr. Tornatore in his initial expert report. (Ex. A, p. 7.) First, Dr. Evans contends that the medical evidence does not suggest that petitioner suffered a detectable stroke and that "if stroke were found it would poorly explain her memory loss." (*Id.*) Dr. Evans notes that isolated memory dysfunction caused by stroke is rare when not accompanied by other signs or symptoms. (*Id.*) Further, when isolated memory loss is present, it is suggestive of bilateral stroke of the medial temporal lobes or thalamus. (*Id.*) Although "multi-infarct dementia" is relatively common in stroke victims, it is usually associated with clinically-diagnosable stroke and accompanied by other signs and symptoms. (*Id.* (citing Alzheimer's Ass'n, *Vascular Dementia* 1–4, (2018) (Ex. D); Didier Leys, *Poststroke dementia*, 4 LANCET NEUROLOGY 752 (2005) (Ex. R)).) Dr. Evans notes that petitioner's radiographic imaging did not reveal signs of a stroke, but rather a very common and nonspecific finding of "minimal periventricular white matter demyelinization likely from chronic small vessel ischemic disease" regularly found in middle aged, elderly, and

[7] Dr. Evans acknowledges there are some cases of vaccine-associated encephalopathy and severe seizures in children, but that "[t]hese mostly turned out to be cases of Dravet syndrome (severe myoclonic epilepsy of infancy) with the first symptoms precipitated by malaise and fever after vaccination." (Ex. A, p. 6.) However, Dravet syndrome is usually caused by a mutation in the SCN1A gene. (*Id.* (citing Tarannum M. Lateef et al., *Seizures, encephalopathy, and vaccines: experience in the national vaccine injury compensation program*, 166 J. OF PEDIATRICS 575 (2015) (Ex. Q); Lieve Claes et al., *De novo SCN1A Mutations are a major cause of severe myoclonic epilepsy of infancy*, 21 HUM. MUTATION 615 (2003) (Ex. J)).) Dr. Evans stresses that in these cases, "vaccination did not cause but did appear to precipitate the first observable seizures of a catastrophic genetically-determined epilepsy," with similar precipitation of seizures observed in other childhood epilepsies such as Doose syndrome. (*Id.* (citing Samuel F. Berkovic et al, *De-novo mutations of the sodium channel gene SCN1A in alleged vaccine encephalopathy: a retrospective study*, 5 LANCET NEUROL. 488 (2006) (Ex. H); Natasha J. Brown et al., *Vaccination, seizures and 'vaccine damage'*, 20 CURR. OP. NEUROL. 181 (2007) (Ex. I); Nienke E. Verbeek et al., *Etiologies for seizures around the time of vaccination*, 134 PEDIATRICS 658 (2014) (Ex. Y); Sarah von Spiczak et al., *A retrospective population-based study on seizures related to childhood vaccination*, 52 EPILEPSIA 1506 (2011) (Ex. Z)).)

hypertensive persons at a rate of 50-98%. (Ex. A, p.7 (citing Vincent Mok et al., *Race-ethnicity and cerebral small vessel disease – Comparison between Chinese and white populations*, 9 INT'L J. OF STROKE 36 (2014) (Ex. T)).) Dr. Evans notes that, while chronic small vessel ischemic disease is not known to cause symptoms by itself, it has been correlated with increased dementia and demyelinating lesions in dementia patients. (Ex. A, p. 7 (citing Doeschka A. Ferro et al., *Clinical relevance of acute cerebral microinfarcts in vascular cognitive impairment*, 92 NEUROLOGY e1 (2019) (Ex. L)).) Finally, although confluent demyelination has been associated with vascular dementia, Dr. Evans notes that petitioner's MRI showed minimal, and not confluent demyelination, and therefore, petitioner is unlikely to have suffered from vascular dementia. (Ex. A, p. 7.)

Dr. Evans concludes that in contrast to ischemic disease, where isolated memory dysfunction rarely occurs, it is quite common in temporal lobe epilepsy. (*Id.*) Further, petitioner's EEG was highly suggestive of right temporal lobe epilepsy. (*Id.*) Dr. Evans writes that Dr. Tornatore was mistaken to suggest that the two most common causes of EEG changes are tumor and ischemic disease, because the most common cause of EEG changes is epilepsy which "may in turn be associated with ischemic disease or tumor, and both increase the risk of epilepsy." (*Id.*) Dr. Evans ultimately opines that petitioner's correct diagnosis was epilepsy but that it is highly unlikely to have been caused by her vaccination and could have been triggered by fever or petitioner's viral syndrome. (*Id.*)

In his supplemental expert report, Dr. Evans suggests that petitioner's complaints of "cloudy thoughts" and "not being able to get it together" were cognitive, not behavioral, complaints that preceded her vaccination. (Ex. CC, p. 1 (citing Ex. 5, p. 23; Ex. 11, p. 35).) Dr. Evans agrees that petitioner was correctly diagnosed with epilepsy, but reiterates that petitioner's MRI finding of chronic small vessel ischemic disease is very common and does not support a finding of symptomatic microvascular disease. (Ex. CC, pp. 1-2.) Dr. Evans agrees that systemic exposure to viral or bacterial elements can precipitate seizures or neuronal irritability, but he stresses that they "precipitate acute symptomatic seizures in non-epileptic patients (rarely) or seizure breakthroughs in epileptic patients (commonly)," and are not expected to cause epilepsy. (*Id.* at 2.) Dr. Evans acknowledges that vaccinations can be temporally associated with epilepsy because they may induce a fever and lower the seizure threshold. (*Id.* at 3.) That fact alone, however, is not enough to infer causation. (*Id.*)

ii. Testimony

Dr. Evans also testified at the entitlement hearing. (Tr. 203-277.) Regarding petitioner's causation theory, and whether vascular disease is caused by inflammation, Dr. Evans cautioned that the term "inflammation" is used commonly in the literature though it holds many different meanings. (*Id.* at 258-59.) In fact, he testified that inflammation is thought to be involved "in almost every neurological disease right now." (*Id.* at 259.) Migraines, spinal cord trauma, brain trauma, as well as epilepsy and stroke and are all associated with inflammatory changes, according to Dr. Evans. (*Id.*) He

testified that whether inflammation causes stroke is up for debate. (*Id.* at 259-60.) Dr. Evans explained that the "ultimate cause" of most stroke is either platelet emboli or fibrin emboli—"[s]o something, whether inflammatory or noninflammatory, causes clots to form on vessels that then embolize to other vessels or cause a large enough clot inside you to occlude blood vessels." (*Id.* at 260.) Other cases may involve chronic, increasingly greater stenosis, causing stroke, though Dr. Evans opines that gradually developing stenosis isn't considered a significant risk factor for stroke. (Tr. 260.) In petitioner's case, no sedimentation rate or CRP tests were performed that could have revealed inflammation in petitioner's central nervous system. (*Id.* at 261.) If Dr. Evans were treating petitioner as a patient, and believed petitioner suffered inflammation of the nervous system, he testified that he would have ordered a lumbar puncture to look for leukocytes or lymphocytes in the spinal fluid, for example. (*Id.*) In petitioner's case none of these tests were done, and according to Dr. Evans, "the obvious reason for that is because they weren't concerned about that." (*Id.*)

Of the case reports cited by petitioner, Dr. Evans testified that only the Thoon and Chan report showed some evidence suggesting the flu vaccine is associated with stroke. (Tr. 263.) The ten-year-old patient suffered a cerebellar stroke post flu vaccination. (*Id.*) However, Dr. Evans stresses that the authors did not test any inflammatory markers or demonstrate any inflammatory marks in that case. (*Id.*) To be sure, the authors performed an MRI scan and EEG. (*Id.*) "So, yes, the patient clearly had a stroke and it clearly showed on MRI, and it clearly happened shortly after a vaccination," but Dr. Evans contends the authors fail to show signs of inflammation that might be the base of physiologic significance. (*Id.*)

During his testimony, Dr. Evans amended his opinion in two regards. First, Dr. Evans testified that he opines petitioner "may have epilepsy." (Tr. 266.) This is not inconsistent with his expert reports, however, at the hearing, he explained that "[i]t's been…two, three years since I wrote my initial opinion on it…I do not disagree with the treating physicians having a working diagnosis of epilepsy. However, three years is plenty of time to reduce the working diagnosis to a certainty, and that hasn't been done." (*Id.*) Moreover, based on the little evidence in favor of epilepsy, Dr. Evans opines "I would not tell her she has epilepsy and not treat her for epilepsy until I have more evidence in favor of epilepsy." (*Id.* at 266-67.) Relatedly, Dr. Evans testified that petitioner's depression, not her provisional diagnosis of epilepsy, is the most likely cause of her memory dysfunction. (*Id.* at 271-72.) He explains that the two diagnoses that would be associated with poor performance on her neuropsychological test (that demonstrated cognitive dysfunction) would be depression or possibly epilepsy. (*Id.*) Again, while epilepsy was a "good working diagnosis in 2019," he stresses it has not been proven in petitioner's case. (*Id.* at 272.) That leaves depression as the most likely cause of her memory dysfunction.

Dr. Evans also amended his opinion regarding the results of petitioner's EEG monitoring. (Tr. 211-12, 216.) In particular, he testified that petitioners first EEG results revealed unilateral discharges. (*Id.* at 211.) The second, later EEG was interpreted as normal. (*Id.*) Dr. Evans testified the first EEG showed temporal lobe discharges, which

is common in temporal lobe epilepsy. (*Id.*) The confusion regarding the EEG stems from the fact that the EEG report indicated right temporal lobe discharges, but Dr. Thomas, one of petitioner's treating neurologists opined that petitioner had left temporal lobe discharges. (*Id.* (discussing Ex. 10, p. 9; Ex. 12, p. 10).) On further examination, Dr. Evans testified that petitioner likely had left temporal lobe discharges because the EEG report specifically mentioned F7 and T3 electrodes were affected, which are electrodes in the left side of the head. (Tr. 211-12.) He concludes that the impression in the report was incorrect. (*Id.* at 212.) Dr. Evans testified that, either way, the results indicated focal epileptic discharges in the temporal lobe. (*Id.*) Focal seizures are considered unilateral, occurring in only one half of the brain. (*Id.*) Given the foregoing, Dr. Evans opines that petitioner did not experience epileptic seizures—what she describes were bilateral hand movements that occurred in the absence of other symptoms. (*Id.*)[8]

VI. Discussion

In light of petitioner's framing of the case, the analysis below utilizes the first three *Loving* prongs to address several key factual predicates to petitioner's claim. However, the resolution of these factual issues is the same regardless of whether petitioner's claim is ultimately analyzed as a significant aggravation under the *Loving* test or as an injury caused-in-fact by vaccination under the *Althen* test. This is primarily addressed within the analysis pursuant to *Loving* prong five/*Althen* prong two, which requires a logical sequence of cause and effect linking the vaccine and the injury under either type of analysis.

a. *Loving* prong one

The first *Loving* prong involves an examination of petitioner's pre-vaccination condition. In this case, two factual points relating to petitioner's pre-vaccination condition help to inform whether petitioner's overall explanation of events is likely. First, petitioner must establish that she had preexisting asymptomatic microvascular angiopathy. (ECF No. 56, p. 11; Tr. 12.) Second, in order to ultimately establish petitioner's epilepsy first arose post-vaccination under *Loving* prong two, petitioner must be persuasive in contending that the cognitive complaints attributable to that epilepsy also first arose post-vaccination. That requires examination of respondent's contention that petitioner's pre-vaccination counseling records document cognitive complaints approximately one month prior to the vaccination at issue. (ECF No. 61, p. 2; ECF No. 60, pp. 23-24.)

[8] However, Dr. Evans also testified that, based on this opinion, the discharges were on the left side could "at least be consistent with that particular symptom of spasm in the right hand" and the "writing discomfort may be related to that." (Tr. 217.) However, he maintains, "[b]ilateral hand symptoms do not make sense." (*Id.*)

i. Asymptomatic microvascular angiopathy

Dr. Tornatore's suggestion that petitioner had preexisting microvascular angiopathy is based on two considerations. (Tr. 15-16, 59.) First, he notes petitioner had risk factors for microvascular disease, including hypertension, obesity, and hyperlipidemia. (*Id.* at 15.) Second, he suggests that petitioner's August 20, 2015 MRI had some evidence of "minimal" abnormality constituting chronic small vessel vascular disease. (Ex. 12, p. 22.) He opines that the changes seen on the MRI would not have happened within the span of a year. Thus, he suggests the changes necessarily predated her vaccination. (Tr. 17.)

Importantly, however, Dr. Tornatore also suggests, based on his interpretation of petitioner's history, that the alleged microvascular angiopathy was having no impact on her health prior to vaccination – "it was not presenting at all." (Tr. 20-21.) In that regard, petitioner's treating neurologists interpreted petitioner's MRI as being "within normal limits" for her age. (Tr. 72-74.) Specifically, Dr. Thomas, the physician that initially ordered the MRI to evaluate petitioner's memory problems, interpreted the resulting MRI as "wnl [within normal limits] for age." (Ex. 12, p. 10.) Subsequently, Dr. Buechel additionally characterized the MRI as "normal." (Ex. 28, p. 32.) Later providers likewise concluded the MRI was essentially normal. (Ex. 28, p. 12 (PA-C Kramer); Ex. 28, p. 10 (Dr. Vanderkolk, indicating "minimal periventricular white matter ischemic changes were seen typical for her age and nothing apparently abnormal by my view.").)

For his part, Dr. Evans limited his opinion because he has not reviewed the MRI and allowed the possibility that the MRI "might be evidence of ischemia," but stressed that what petitioner's treating physicians described is a "very common finding," explaining that "if normal means most people have it, then it would be normal." (Tr. 231-32.) When challenged on cross-examination, Dr. Tornatore maintained that an abnormality was present, but also acknowledged that "I don't disagree" that the findings are normal for someone of petitioner's age. (Tr. 73.)

On the whole, while Dr. Tornatore is persuasive in suggesting that the changes evidenced by the August 20, 2015 MRI are likely to have predated the vaccination given that they are chronic and age-related, he has not preponderantly supported that they are clinically significant.

ii. Cognitive impairment

Prior to vaccination, petitioner sought counseling for mild depression triggered by the passing of her sister and cousin. (Ex. 5, pp. 2-13.) On September 18, 2014, about a month prior to the vaccination at issue, petitioner presented for a psychotherapy session wherein she reported "cloudy thoughts" and "not being able to get it together." (*Id.* at 23.) There is no dispute as to the fact of this report of cognitive complaints. However, in order to support his assertion of a "striking" relationship between petitioner's post-vaccination illness and her cognitive problems, Dr. Tornatore opines

that these reports are entirely unrelated to any subsequent complaints of memory issues.

According to Dr. Tornatore, this pre-vaccination cognitive complaint is distinct from petitioner's later cognitive complaints that were reported post-vaccination because it is grief related and best understood as "pseudodementia," which he characterizes as "where somebody's so depressed that they can't think right." (Tr. 26.) He adds that it is also distinct because it reflects "somebody who has great insight into what their problems are and recognizing it as such." (*Id*.) For his part, Dr. Evans describes pseudodementia as representing depression so profound that it can be misdiagnosed as dementia. (*Id.* at 252-53.) Absent that, Dr. Evans suggests that there is no reliable way to parse petitioner's lay reports of cognitive difficulties. Dr. Evans opines that, whether related to depression or epilepsy, petitioner's pre- and post-vaccination cognitive complaints should be considered together rather than trying to distinguish one type of complaint from another. (*Id*.) Importantly ,Dr. Tornatore does acknowledge that, but for his assessment of the specific context in this case, a report of "cloudy thoughts" could be representative of a cognitive complaint, even in the context of a history of depression. (*Id.* at 149.) In that regard, Dr. Tornatore's assessment of the record as clearly evidencing pseudodementia is not well supported.

Petitioner first presented for therapy related to a "rough patch" in her life in July of 2014. At that time, her initial assessment documented age-appropriate memory and thought processes. (Ex. 5, p. 10.) She was initially assessed as having bereavement, not depression. (*Id*. at 12.) Petitioner was not assessed as having any pseudodementia and no other notations in the therapy records suggest that petitioner was experiencing grief-related cognitive difficulties. Viewing the therapy records as a whole, the September 18, 2014 notation of a cognitive complaint is an isolated instance rather than constituting any clear part of her pattern of depression. Additionally, while her course of therapy was targeted to depression and grief counseling overall, the records reflect discussion of issues that were not limited to grief. The record of the session at which the statements were made indicates that three goals were addressed at that session: "relationship building, grief[,] and current functioning." (*Id*. at 23.) Nor does the record notation in any way suggest that petitioner had "insight" into the nature of her reported difficulties as Dr. Tornatore suggests. Rather, the notation was limited merely to the fact of the cognitive complaint.[9]

[9] Critical to Dr. Tornatore's assessment of the statements at issue are their juxtaposition against other statements in the same record. Specifically, the record states: ". . . CI reports she continues to struggle with the grief related to the loss of her sister and cous[in] approximately a year ago. CI states 'I think they know something is wrong where I work. I cried the other day but did not let anyone see.' CI report 'cloudy thoughts' and 'not being able to get it together.' CI shows pattern of high expectation of herself in multiple areas of her life. CI reports that she is going to make the church she is going to her home church . . ." (Ex. 5, p. 23.) Dr. Tornatore specifically links the statement regarding crying at work to the statements regarding cloudy thoughts; however, given the scope of the reports summarized without transitions in just a few short sentences in this and other session records, Dr. Tornatore is not persuasive in suggesting that the sentence reporting an episode of crying at work must necessarily be related to the following sentence relating to the clarity of her thoughts.

Further, petitioner's overall medical records do not clearly reflect the distinction Dr. Tornatore raises between petitioner's pre- and post-vaccination cognitive complaints. Whereas the reference to "cloudy thoughts" and "not being able to get it together," are an isolated instance within the therapy record, this complaint was made only one month prior to what petitioner otherwise contends became an ongoing pattern of memory loss. In fact, petitioner's first report of post-vaccination symptoms on October 27, 2014, employed language very similar to the prior therapy record in reporting that petitioner "can't think." (Ex. 6, p. 2.) It was not until she returned for follow up that this was specifically noted to be an issue of memory. (*Id*. at 3 ("memory still bothersome").) Moreover, consistent with "cloudy thoughts" and "not being able to get it together," when petitioner later presented for a vocational assessment, she was noted to have both memory impairment and executive function difficulty. (Ex. 24.) Thus, even if petitioner subjectively believed at the time that she was reporting grief related cognitive difficulties to her therapist in September of 2014, Dr. Evans is persuasive in suggesting that there is little to no medical basis for parsing petitioner's earliest cognitive complaints from her later cognitive complaints. (Tr. 252-53.)

For all these reasons, Dr. Tornatore is not persuasive in suggesting that the notations in petitioner's contemporaneous therapy records demonstrate her pre-vaccination cognitive complaints to be of a distinctly different character. Thus, Dr. Tornatore is not persuasive in dismissing petitioner's pre-vaccination report of "cloudy thoughts" and "not being able to get it together" as a separate pseudodementia unrelated to her subsequent cognitive complaints.

b. *Loving* prong two

The second *Loving* prong examines petitioner's post-vaccination condition. In order for petitioner's preferred explanation of events to be likely, she must preponderantly prove three underlying points with respect to her post-vaccination condition. First, she must establish that she does suffer epilepsy. Second, if she does suffer epilepsy, then she must establish that onset of any seizure disorder was after the time of the acute-post-vaccination cerebral vascular event that allegedly caused it. Third, and relatedly, she must demonstrate that she actually suffered an acute cardiovascular event.

i. Epilepsy

On September 8, 2015, petitioner underwent EEG which was abnormal due to sharp waves concerning for an epileptogenic focus. (Ex. 10, p. 10.) Dr. Thomas initially suspected subclinical seizures and later records accept a history of focal epilepsy. (Ex. 12, p. 10; Ex. 28, p. 10.) Thus, Dr. Tornatore endorses a seizure disorder. (Tr. 12.) Respondent disputes that any epilepsy diagnosis is preponderantly established (ECF No. 60, pp. 10-12); however, his own expert agrees that petitioner's EEG demonstrated epileptic discharges and that "I don't disagree with the clinician's diagnosis of possible subclinical seizures causing memory problems. That's typical. Memory loss is very commonly associated with epilepsy." (Tr. 219.) Although Dr. Evans has significant

doubts that there is sufficient clinical evidence to confirm the diagnosis, he agrees that it is "more than possible" and "quite plausible." (Tr. 219-21.)

In light of all of the above, while it is not certain that petitioner suffers epilepsy, I conclude that petitioner has established that there is preponderant evidence that she suffers left temporal focal epilepsy.

ii. Epilepsy/seizure onset

Although the fact of petitioner's epilepsy is preponderantly established, a post-vaccination seizure onset is not. As noted above, petitioner's epilepsy was first documented in connection with her September 8, 2015 EEG, about a year post-vaccination. (Ex. 10, p. 9.) At that time, it was viewed as a possible explanation for her memory problems dating back earlier. (Ex. 12, p. 10.) In that regard, both Dr. Tornatore and Dr. Evans agree. (Tr. 35-36, 107, 219.)

However, Dr. Evans explained that the discharges seen on EEG are only biomarkers of epilepsy. They are not evidence of seizures in themselves. (Tr. 223.) Moreover, while seizures typically include temporary amnesia during the seizure and post-ictal period, permanent memory loss like that displayed by petitioner would take "lots and lots of seizures over years" and it "doesn't happen overnight or quickly." (*Id.* at 223-24.) Thus, even accepting *arguendo* that her memory complaints began shortly after vaccination, her epilepsy would have begun much earlier. Additionally, for the reasons discussed under *Loving* prong one, above, petitioner actually began complaining of cognitive concerns no later than about a month prior to her vaccination. All of this strongly suggests that, if petitioner had epilepsy-related permanent memory loss as alleged, then the epilepsy must have been chronic and preexisted her vaccination.

Dr. Tornatore cites petitioner's hand spasms, which were first documented post-vaccination, as evidencing seizure activity. (Tr. 28, 101-03.) However, petitioner's own treating physician, Dr. Buechel, specifically opined that the hand spasms were not related to seizures. (Ex. 28, p. 32.) Furthermore, Dr. Evans persuasively explained that the hand spasms are not consistent with petitioner's EEG, because they manifested bilaterally.[10] (Tr. 210-12.) The focal discharges evidenced by the EEG would not result in bilateral symptoms and in the absence of other symptoms, bilateral hand movements "is not a seizure semiology." (*Id*. at 212.) It would also be unusual for petitioner to be aware of her hand spasming if they were in fact seizures, because seizures generally involve temporary amnesia. (Tr. 223.) This latter point also appears to have partly informed Dr. Buechel's opinion. (Ex. 28, p. 32.)

[10] Petitioner's separate symptom of right hand cramping could potentially be consistent with left focal discharges insofar as the bilateral presentation would not be an issue (Tr. 216-17); however, the other issues would remain and petitioner's treating physician felt this was due to "organic writer's cramp." (Ex. 28, p. 35.)

In light of all of this, there is not preponderant evidence that petitioner ever suffered a clinically apparent seizure, meaning her epilepsy only ever consisted of subclinical seizures. It is therefore not possible to identify the initial onset of the epilepsy on this record. However, to the extent the epilepsy is viewed as the cause of petitioner's memory problems, this would likely place the onset of epilepsy *prior to* the vaccination at issue, especially, but not only, because of the analysis of petitioner's cognitive complaints under *Loving* prong one.

iii. Acute cerebrovascular event

One of petitioner's treating physicians, Dr. Thomas, questioned whether petitioner may have experienced an acute cardiac episode such as a stroke or hypertensive event. (Ex. 12, p. 17.) This was not based on any direct evidence, but rather upon the seeming coincident nature of petitioner's post-vaccination illness and her reports of cognitive complaints. (*Id*.) The assessment was first notated prior to petitioner undergoing the MRI study that Dr. Thomas would later interpret as being within normal limits for age. (*Id*. at 10.) The majority of petitioner's treating physicians, including her other neurologists, offered no such opinion. Apart from her reported cognitive complaints, petitioner never presented for care with symptoms of a stroke. (Tr. 236-39, 246-48.) Based on Dr. Evan's assessment, a stroke would be implausible given petitioner's history. (*Id*. at 249.)

Nonetheless, Dr. Tornatore applies the same reasoning as Dr. Thomas. During the hearing, Dr. Tornatore acknowledged that petitioner's MRI scan itself is incapable of detecting whether any acute event had previously happened. (*Id*. at 20.) Rather, to the extent it is interpreted abnormal at all, it reflects only chronic changes. However, he felt the abrupt timing of onset of petitioner's seizures and memory problems following petitioner's constitutional symptoms supported the existence of an acute cardiovascular event. (*Id*. at 56-58.) Following resolution of the above-discussed facts, this opinion is not tenable.

Because petitioner's epilepsy was only ever subclinical, there is no evidence to support that a seizure disorder began after petitioner's constitutional symptoms. To the extent her cognitive complaints are attributable to epilepsy, there is also not preponderant evidence clearly placing onset of those cognitive complaints post-vaccination as petitioner alleges. Without persuasive evidence supporting Dr. Tornatore's preferred coincident timing, there is no basis to speculate that any acute cardiovascular episode ever occurred. Dr. Tornatore acknowledged that the type of cognitive difficulties at issue in this case can be the result of accumulated damage. (Tr. 74.) Thus, even if petitioner had demonstrated her preexisting microvascular angiopathy to have been clinically significant, and even if it were a contributor to petitioner's epilepsy (a point Dr. Evans would dispute (Tr. 275)), this would still not imply the presence of any acute cerebrovascular event.

Furthermore, Dr. Tornatore acknowledged that, to the extent he characterizes acute ischemia as a stroke, if a stroke occurred, it was a "small" stroke. (Tr. 65.)

However, Dr. Evans explained that typically when a minor stroke causes later epilepsy, the epilepsy arises months after the stroke. (Tr. 226.) In order for a stroke to acutely cause epilepsy as proposed by Dr. Tornatore, it would most likely have to be of a severity that would be "obvious" and detectable on MRI, even an MRI performed as remotely as the MRI available in this case. (Tr. 226-29, 240, 245.)

c. *Loving* prong three

Under *Loving* prong three, a comparison of the pre- and post-vaccination conditions examined under the first two prongs must indicate that petitioner has experienced a change for the worse in her pre-existing condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health. § 300aa-33(4). This aspect of the analysis does not reach the question of vaccine-causation and petitioner is not obligated to show that her outcome is worse than the expected outcome for a person with her condition. *Sharpe v. Sec'y of Health & Human Servs.*, 964 F.3d 1072, 1081-82 (Fed Cir. 2020).

In this case, petitioner's claim is that she ultimately suffers cognitive issues related to epilepsy. It is beyond meaningful dispute that petitioner's cognitive condition is worse post-vaccination than it was pre-vaccination. However, the pre-existing condition petitioner alleges to have been worsened is her alleged asymptomatic microvascular angiopathy. Thus, based on petitioner's framing of the issues in this case, *Loving* prong three turns on whether petitioner has shown that her alleged epilepsy is a sequela of her cardiovascular health. (In her brief, petitioner characterizes this as whether her preexisting microvascular angiopathy "evolved into" epilepsy. (ECF No. 56, p. 11).)

While epilepsy can be a sequela to ischemic disease, that is certainly not the only cause and new onset of epilepsy in adults is "not rare."[11] (Ex. A, pp. 6-8.) Dr. Tornatore's opinion is based on the "striking" nature of petitioner's clinical presentation and his assertion that "it doesn't make sense" that petitioner's post-vaccination constitutional symptoms (*i.e.* her diagnosed viral syndrome) and cognitive complaints would arise at the same time, but be unrelated. (Tr. 56-57.) Here, however, a comparison of the separate analyses discussed relative to *Loving* prongs one and two above finds that petitioner has not preponderantly shown that this striking coincidence occurred or that her epilepsy is related to any prior microvascular angiopathy

First, petitioner has not preponderantly shown either under *Loving* prong one that her preexisting microvascular disease was clinically significant in the first place or under *Loving* prong two that she suffered any acute cardiovascular event following her vaccination. While Dr. Evans agrees that either stroke or "extensive" ischemic disease can cause epilepsy, he explained that a mild chronic small vessel ischemic disease is not associated with epilepsy. (Tr. 275; Ex. CC, pp. 2-3.)

[11] Petitioner did report a family history of epilepsy. (Ex. 28, p. 32; Ex. 12, p. 15 (noting petitioner has a brother who had epilepsy since childhood).)

Second, petitioner has not demonstrated under *Loving* prong one she was free of cognitive difficulties pre-vaccination nor under *Loving* prong two that she suffered overt seizures post-vaccination. Thus, the actual onset of her epilepsy, which has remained subclinical, is unknown, and may well have begun prior to vaccination.

For these reasons, petitioner has not preponderantly demonstrated that her cerebrovascular health deteriorated post vaccination nor that her epilepsy was caused by any post-vaccination acute cerebrovascular event. Thus, petitioner's epilepsy and its consequences do not constitute a significant aggravation of microvascular angiopathy. Petitioner therefore has not preponderantly satisfied her burden under *Loving* prong three.

d. *Althen* prong one/*Loving* prong four

i. Petitioner's burden of proof

Petitioner's burden under the first *Althen* prong/fourth *Loving* prong is to provide, by preponderant evidence, "a medical theory causally connecting the vaccination and the injury." *Althen,* 418 F.3d at 1278. Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Human & Health Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994). Moreover, scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1380 (Fed. Cir. 2009). However, to satisfy this prong, petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548; *Boatmon*, 941 F.3d at 1359. Petitioner's burden under *Loving* prong four varies from her burden under *Althen* prong one in that a significant aggravation claim requires petitioner only to show that the vaccine at issue can worsen the condition at issue rather than being its cause. *Sharpe*, 964 F.3d at 1083 (explaining that "[u]nder *Loving* prong 4, a petitioner need only provide 'a medical theory causally connecting [petitioner]'s significantly worsened condition to the vaccination.' In other words, Petitioner was required to present a medically plausible theory demonstrating that a vaccine 'can' cause a significant worsening of [petitioner's injury].")

Petitioner's prehearing brief includes a recitation of the applicable legal standard comparable to the above. However, she urges that her burden under *Althen* prong one/*Loving* prong four is specifically limited to a showing of "biologic plausibility" based on a more recent Court of Federal Claims decision. (ECF No. 56, p. 10 (quoting *J. v. Sec'y of Health & Human Servs.*, 155 Fed. Cl. 20, [pin pg] (2021).) In sum, petitioner argues that in 2009 the Federal Circuit in *Andreu* articulated "biological plausibility" as the standard for evaluating a theory pursuant to *Althen* prong one and that this articulation has never been overturned.[12] (ECF No. 56, p. 10.) Importantly, however,

[12] A subsequent Court of Federal Claims decision has come to a different conclusion following a review of the same prior precedents. *K.A. v. Sec'y of Health & Human Servs.*, 164 Fed. Cl. 98, 125-26 (2022) (characterizing petitioner's reliance on a "biologically plausible" standard as an attempt to "refashion the

this does not indicate that a theory must be couched or addressed specifically by that terminology. The Federal Circuit has explained in *Knudsen* that "[c]ausation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules." 35 F.3d at 548. Regardless of the specific reference to "biologic plausibility," the Federal Circuit's decision in *Andreu* explains that a petitioner's burden is to provide a theory "supported by a 'reputable medical or scientific explanation.'" 569 F.3d at 1379 (quoting *Althen*, 418 F.3d at 1278).) The Circuit further explained that the assessment of whether a theory is reputable "can involve assessment of the relevant scientific data" but stressed that such an assessment must be based on preponderant evidence as contrasted against the type of "very near certainty – perhaps 95% probability" generally required by medical research. (*Id.* at 1380.) Nothing in *Andreu* implies that the "biologically plausible" theory presented in that case constituted anything less than preponderant evidence or that a theory that is not "sound and reliable" could be considered "biologically plausible." While scientific certainty is clearly *not* required, the Federal Circuit has also repeatedly held that theories that are "plausible," as in merely "possible," do not meet petitioner's preponderant burden of proof. *Boatmon*, 941 F.3d at 1360.

ii. Application to Dr. Tornatore's opinion

During the hearing, Dr. Tornatore summarized his causal opinion as follows: "[P]etitioner had underlying microvascular angiopathy as seen by her MRI . . . there was a [flu] vaccination that she received . . . that resulted in cytokine and chemokine release, which in turn led to small vessel changes . . . leading to either contraction or frank ischemia in the small [] blood vessels, which led to a scar, which in turn led to neuronal irritability, and then the more permanent seizure disorder thereafter with the memory and the cognitive issues being part of the symptomology." (Tr. 35-36.) In other words, Dr. Tornatore's theory of vaccine causation is that the cytokine response to vaccination can cause cardiovascular changes resulting in stroke.[13] Stroke, in turn, can then explain this petitioner's clinical history.

Several of the points contributing to Dr. Tornatore's theory are not disputed. Dr. Evans agrees that epilepsy can cause permanent memory loss. (Tr. 219, 223.) He also agrees that a stroke can cause epilepsy. (*Id*. at 224.) In fact, he characterizes it as "very common." (*Id*.) Further, Dr. Evans agrees that strokes are associated with inflammation. (*Id*. at 259-60.) The question on which the experts disagree is whether the flu vaccine itself can cause or trigger a stroke. (*Id*. at 262-63.)

---

first *Althen* prong standard" and citing approvingly to the "sound and reliable" language included in the Federal Circuit's *Boatman* decision).

[13] During cross-examination, Dr. Tornatore seemed to characterize his opinion as being based on either "ischemic events or strokes." (Tr. 64.) However, he also provided testimony suggesting that he is using the terms interchangeably, stating "any way you look at it, this is vascular disease, and it would be considered a stroke." (Tr. 65.) Asked if his opinion is that petitioner had "an acute stroke," he answered "Yes, I think there was an acute event that happened . . ." (Tr. 67.) On further questioning he indicated that stroke is "too generic" and that "vascular event" gets closer to what he opines happened; however, he was clear in expressing that his theory requires an event causing permanent damage, as opposed to a hypertensive urgency or PRES, which were also referenced by Dr. Thomas. (Tr. 172-78.)

As a starting point, Dr. Tornatore relies on a 2002 review article by Libby, et al., positing a relationship between inflammation and atherosclerosis (*i.e*. the deposition of fatty plaques on artery walls). (Libby et al., *supra*, at Ex. 18.) The authors suggest that atherosclerosis should not be viewed merely as a bland lipid storage disease. (*Id*. at 1.) Instead, they conclude that "[c]urrrent evidence supports a central role for inflammation in all phases of the atherosclerotic process." (*Id*. at 7.) The authors further suggest that "[c]irculating acute-phase reactants elicited by inflammation may not only mark increased risk for vascular events, but in some cases may contribute to their pathogenesis." (*Id*.) This is characterized as being a "new insight" at the time. (*Id*.) Importantly, however, this paper discusses inflammation as arising in the context of otherwise accepted risk factors for cardiovascular disease, including obesity, hypertension, diabetes, and infection. (*Id*. at 3-4.) Notwithstanding his citation to outlier cases, Dr. Tornatore acknowledged that for most patients there is a difference in the potency of the immune response to vaccination as compared to infection and that infection would be a more likely cause of the type of inflammatory cascade he proposes. (Tr. 145, 158.) Nothing in the Libby, et al., paper implicates vaccinations broadly or the flu vaccine specifically as a cause of stroke.

In contrast, it is undisputed that the flu vaccine has been shown epidemiologically to have a cardio-protective effect. (Armin J. Grau et al., *Influenza Vaccination is Associated with a Reduced Risk of Stroke*. 36 STROKE 1501 (2005) (EX. 32); Nichols et al., *supra,* at Ex. EE; Philippa Lavallee et al., *Association Between Influenza Vaccination and Reduced Risk of Brain Infarction*, 33 STROKE 513 (2002) (Ex. DD).) This is not dispositive, but provides some important context. *Accord Baldwin v. Sec'y of Health & Human Servs*., No. 13-957V, 2020 WL 4197937, at n. 14 (Fed. Cl. Spec. Mstr. June 4, 2020) (explaining that because influenza infection is associated with increased deaths from cardiovascular disease "assessment of the true significance of this epidemiologic evidence [is] very difficult. Accordingly, epidemiologic evidence of a cardio protective effect from the influenza vaccine, though relevant, is not in itself dispositive"), *mot. rev. denied,* 151 Fed. Cl. 431 (2020). The Federal Circuit has previously stressed that a petitioner is not obligated to present an epidemiological case supporting her claim. *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). Nonetheless, "[n]othing in *Althen* or *Capizzano* requires the Special Master to ignore probative epidemiological evidence that undermines petitioner's theory." *D'Tiole v. Sec'y of Health & Human Servs.*, 726 F. App'x 809, 811 (Fed. Cir. 2018) (citing *Andreu*, 569 F.3d at 1379 ("Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the Special Master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury.").

Set against the lack of epidemiologic support for this theory, Dr. Tornatore provides three studies seeking to establish that the flu vaccine does create a cytokine response that can vary depending on individual characteristics, such as age or pre-existing conditions. (Carty et al., *supra* at Ex. 20; McDonald et al., *supra,* at Ex. 19;

Talaat et al., *supra,* at Ex. 35.) However, none of these studies demonstrates that this cytokine response leads to relevant adverse events. Of the three, only Carty et al., specifically examined cardiovascular health, comparing post-vaccination cytokine levels in those with preexisting carotid artery disease against controls without the disease. Although the group with preexisting disease had higher cytokine levels, individuals from both groups had "mild, but measurable" levels. Additionally, the authors did not record any adverse events attributable to elevated cytokine levels for either group. (Carty et al., supra, at Ex. 20, p. 1 (abstract).) McDonald, et al., focused on vaccine efficacy using a mouse model. (McDonald et al., supra, at Ex. 19.) Talaat, et al., reported an association between adverse events and cytokine levels post-vaccination. However, the adverse events examined were non-severe and are in no way comparable to what is hypothesized in Dr. Tornatore's theory. About half of the subjects in their study reported either post-vaccination myalgia or injection site pain, which were described most often as mild. Single subjects reported adverse events such as abnormal sweating (diaphoresis); sore throat; vomiting; and syncope during a blood draw. (Talaat et al., supra, at Ex. 35, p. 5.)

An additional study sought to examine whether response to vaccination could contribute to endothelial dysfunction that could lead to the risk of cardiovascular events. (Aroon D. Hingorani et al., *Acute Systemic Inflammation Impairs Endothelium-Dependent Dilatation in Humans*, 102 CIRCULATION 994 (2000) (Ex. 33).) Subjects were administered a vaccination against Salmonella typhi. Subsequently, the subjects were tested to measure cytokine levels, resistance blood vessel response, and conduit vessel response. The results showed a progressive rise in cytokines, but with no effect on blood pressure, resting heartrate, or baseline forearm blood flow. (*Id*. at 2.) Nonetheless, the results showed "profound, but temporary, suppression of endothelium-dependent relaxation in the forearm circulation. These findings demonstrate that even a relatively mild systemic inflammatory response is associated with significant alteration in endothelial function of a type commonly thought to be associated with increased cardiovascular risk." (*Id*. at 3.) The authors explained, however, that the mechanism by which inflammation may be acting to impair endothelium-dependent relations is not understood and would require further study. (*Id*. at 5-6.) Moreover, the authors acknowledge that the systemic inflammation that has been implicated by infective disorders is "far more severe and long lasting." Although the study demonstrates that even mild inflammation disturbs endothelial regulation, it is yet to be determined whether the observations of the study are seen in a clinical context. (*Id*.)

Apart from these studies, Dr. Tornatore presents two case reports of stroke following influenza vaccination. "[C]ase reports 'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value'…. [but] 'the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight.'" *See Paluck v. Sec'y of Health & Human Servs.,* 104 Fed. Cl. 457, 475 (2012) (quoting *Campbell v. Sec'y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011), *aff'd* 786 F.3d 1373 (Fed. Cir. 2015)).

In the first case report, the authors reported on a 75-year-old male who suffered posterior circulation ischemia after receiving an H1N1 flu vaccination. (Lin et al., *supra,* at Ex. 21).) The patient began experiencing episodes of spontaneously resolving dizziness and unsteady gait on the left side beginning about seven hours after vaccination. He did not seek care until seven days later when MRI showed indications of new infarctions. The authors acknowledge that "[t]he causal relation between vaccination and ischemic stroke is seriously challenged . . . especially when our patient does have a few stroke risk factors, such as hypertension, previously stroke, intracranial atherosclerosis, old age, and hypertriglyceridemia." (*Id*. at 2.) The authors hypothesize that "an inflammatory/immunological response after vaccination may trigger thrombosis superimposing a pre-existing prothrombotic state (*Id*. at 1 (abstract)), but ultimately acknowledge that "it is uncertain if an enhancement of inflammatory/immunological activity after vaccination is sufficient for initiating symptomatic vascular occlusion" (*Id*. at 4).

In the second case report, Thoon and Chan report on a 10-year-old child who suffered a cerebellar stroke one day after receiving the seasonal trivalent influenza vaccine. (Thoon & Chan, supra, at Ex. 31.) Contrasting this case against limited prior case reports involving older individuals with other stroke risk factors, the authors note that their evaluation of this patient did not reveal any underlying prothrombotic conditions. (*Id*. at 4.) Contrasting this case against limited prior case reports involving post-vaccination stroke in children, this patient did not have any imaging consistent with cerebral angiopathy to explain the nature of the ischemic stroke. (*Id*.) The authors ultimately conclude that "[t]he close temporal relationship between an ischemic stroke in an otherwise healthy 10-year-old child with recent receipt of seasonal influenza vaccination may be entirely coincidental, and does not alter our stance in recommencing the influenza vaccination for all children, especially those at risk of developing complications from an influenza infection." (*Id*. at 4-5.)

In sum, petitioner has provided some evidence to suggest a possible role for mostly chronic or infection-related inflammation in contributing to stroke. Petitioner has also provided some experimental evidence to suggest that at least one vaccine not at issue in this case - Salmonella typhi – can affect human blood vessels to at least some degree in an experimental context, though the actual clinical significance of that finding, if any, is unclear. Further to that, petitioner has presented some evidence to support the uncontroversial point that the flu vaccine produces an inflammatory cytokine response, but without any evidence this results in relevant adverse events. Thus, evidence directly suggesting that a flu vaccination itself can result in stroke consists only of two tentative and unsimilar case reports set against epidemiologic data that fails to detect the flu vaccine as carrying a risk for stroke.

Considering all of this collectively and in the context of the record as a whole, I conclude that this is inadequate to preponderantly establish that the flu vaccine can cause a worsening of preexisting microvascular angiopathy leading to or otherwise causing stroke or other acute ischemic event. Thus, petitioner has not preponderantly satisfied *Althen* prong one/*Loving* prong four.

e. *Althen* prong two/*Loving* prong five

The second *Althen* prong/fifth *Loving* prong requires proof of a logical sequence of cause and effect showing that the vaccine was the reason for the injury, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano.*, 440 F.3d at 1317, 1326; *Grant*, 956 F.2d at 1148. However, medical records and/or statements of a treating physician do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. *See* 42 U.S.C. §300aa-13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) (stating that "there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

In this case, analysis of *Althen* prong two/*Loving* prong five begins with petitioner's initial post-vaccination illness. On October 27, 2014, petitioner presented for care at a community clinic with a complaint of six days of illness consisting of loss of appetite, cough, fever and "no energy," but with no sore throat. (Ex. 6, p. 2.) It was noted as part of the history that this illness arose about three hours after her flu vaccination, however, she was diagnosed as having a "viral syndrome." (*Id.*) Petitioner returned for follow up twice and the diagnosis of viral syndrome was never altered. (*Id*. at 3-4.) Significantly, a vaccine reaction was questioned ("flu vaccine?" listed with allergies (Ex. 6, p. 5)), but a viral syndrome with complications was instead diagnosed (*Id*.). According to Dr. Tornatore, this episode should be revisited as a cytokine response to vaccination. (Tr. 27-30.) Dr. Tornatore suggests that, in severe cases, a cytokine response to vaccination can mimic a viral infection. (*Id*. (citing L'Huillier et al., *supra*, at Ex. 34).) However, the L'Hullier paper he cites for this point examines only cytokine levels and does not address the symptoms associated with a cytokine response to vaccination. (L'Huillier et al., *supra*, at Ex. 34.)

In petitioner's case, Dr. Tornatore focuses on constitutional symptoms of fever and chills as well as local injection-site swelling as being consistent with a cytokine response. (Tr. 27-30.) Importantly, however, petitioner's actual treatment records for this illness did not record the injection site swelling she later included in her affidavit account. (*Compare* Ex. 6 (treatment records) and Ex. 25 (petitioner's affidavit).) Petitioner did not report that her arm swelled until she sought care from Dr. Thomas in August of 2015, about ten months post-vaccination. (Ex. 12, p. 15.) However, the records reflect that petitioner's account had changed in multiple ways over time, tending toward petitioner's subjective belief that her vaccination was ultimately responsible for her circumstances. For example, at the time petitioner first presented to Dr. Thomas in August of 2015 and thereafter, she indicated that her post-vaccination illness had resulted in her being fired for being unable to do her job. (Ex. 12, p. 15.) However, in her more contemporaneous therapy records she discussed both her firing and her post vaccination illness without linking the two, instead attributing her firing to "politics" related to an interpersonal conflict at work. (Ex. 5, p. 25.) Additionally, the

hallucinations and visual changes she would later retrospectively report beginning in the summer of 2015 were not documented in any of petitioner's medical records from the autumn of 2014. (Exs. 5-6.) Thus, Dr. Tornatore's assumption of injection site swelling as a tell-tale of a vaccine reaction, for which there is no contemporaneous evidence, is not well supported. *See e.g.*, *R.K. v. Sec'y of Health & Human Servs.*, No. 03-632V, 2015 WL 10936124, at *76 (Fed. Cl. Spec. Mstr. Sept. 28, 2015) (holding that more remote histories of illness do not have sufficient indicia of reliability to be credited over conflicting contemporaneous medical records and earlier reported histories), *mot. rev. denied* 125 Fed Cl. 57 (2016), *aff'd* 671 Fed. Appx. 792 (Fed. Cir. 2016); *see also e.g.*, *Vergara v. Sec'y of Health & Human Servs.*, 08-882V, 2014 WL 2795491, *4 (Fed. Cl. Spec. Mstr May 15, 2014) ("Special Masters frequently accord more weight to contemporaneously-recorded medical symptoms than those *recorded in later medical histories*, affidavits, or trial testimony" (emphasis added).).

Nor does Dr. Tornatore persuasively account for the fact that both petitioner's contemporaneous medical record and her own affidavit confirm that her core symptoms included cough. (Ex. 6, p. 2; Ex. 25, p. 2.) Dr. Evans, by contrast, testified that petitioner's cough is consistent with a viral illness, but not a vaccine reaction. (Tr. 256.) Dr. Tornatore relies on the prescribing information ("package insert") for the Fluzone Quadrivalent vaccine as support for the notion that a cough could be consistent with a vaccine reaction. (Tr. 278-79; Ex. 36.) The package insert lists adverse reactions for four different age groups. For none of the groups is either cough or any upper respiratory complaint listed as an adverse reaction. For adults the most common adverse events were injection site pain, myalgia, headache, and malaise. (Ex. 36, pp. 6-7.) Instead, Dr. Tornatore relies on a discussion of the clinical trials for the vaccine. Specifically, the clinical trials disclose that "cough" was among the most commonly reported unsolicited non-serious adverse events. (Tr. 279-80; Ex. 36, p. 11.) Importantly, however, the package insert cautions against using the adverse event rates as reflecting "the rates observed in practice." (Ex. 36, p. 7.) Additionally, the rates for each of the listed unsolicited adverse events (headache, cough, and oropharyngeal pain) is not specified. All that is indicated is that 33 people reported such events and that this was lower than what was reported among either of the two control groups who received different vaccines. (*Id*. at 15.) Nothing in the document suggests that any significance was found in the reports of cough. Thus, for example, cough was not observed as an adverse event in the Talaat study that Dr. Tornatore relied upon to support his theory that vaccine-related inflammation can lead to acute cardiovascular events. (Talaat et al, *supra,* at Ex. 35, p. 5.) Moreover, nothing in the document explains whether these reports of cough occurred in the context of broader illnesses such as what petitioner experienced.

Both of these points – the cough and the failure to initially report injection site swelling - accord with the diagnosis of the treating physician, who considered, but rejected, a vaccine reaction in favor of a diagnosis of viral syndrome. There is therefore not preponderant evidence that petitioner's contemporaneous diagnosis of a viral syndrome should be set aside in favor of an undiagnosed post-vaccination cytokine response. Absent this, Dr. Tornatore's theoretical causal chain is broken with respect to

any link to vaccination regardless of the resolution of any of the other factual issues in the case. In that regard, Dr. Tornatore agrees that an infection would be capable of setting off the series of events underlying his theory of causation. (Tr. 157.) Similarly, Dr. Evans has opined that, even if petitioner did suffer epilepsy beginning shortly after her these events, it is more likely that it was brought on simply by the infection documented in her medical records. (Ex. A, p. 8.)

Additionally, as explained under *Loving* prong three, temporal lobe epilepsy occurs in the absence of any ischemia. Moreover, for the reasons explained under *Loving* prong one, it is not clear that petitioner's minimal, age-related MRI changes are indicative of any meaningful ischemic disease. And, as explained under *Loving* prong two, there is not preponderant evidence petitioner suffered an acute cerebrovascular event. And, in any event, petitioner's epilepsy more likely predated either her vaccination or her alleged acute cerebrovascular event. Thus, there is little linking petitioner's epilepsy to her cardiovascular health other than Dr. Tornatore's say-so, which is based on assumptions that are not supported by preponderant evidence. *Burns v. Sec'y of Health & Human Servs.*, 3 F. 3d 415 (Fed. Cir. 1993) (holding that "[t]he special master concluded that the expert based his opinion on facts not substantiated by the record. As a result, the special master properly rejected the testimony of petitioner's medical expert."); *see also Rickett v. Sec'y of Health & Human Servs.,* 468 Fed. Appx. 952, 958 (Fed. Cir. 2011) (holding that "it was not error for the Special Master to assign less weight to Dr. Bellanti's conclusion regarding challenge-rechallenge to the extent it hinged upon Mr. Rickett's testimony that was inconsistent with the medical records."); *Dobrydnev v. Sec'y of Health & Human Servs.,* 566 Fed. Appx. 976, 982–83 (Fed. Cir. 2014) (holding that the special master was correct in noting that "when an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion") (citing *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993)); *Bushnell v. Sec'y of Health & Human Servs.,* No. 02-1648V, 2015 WL 4099824, at *12 (Fed. Cl. Spec. Mstr. June 12, 2015) (finding that "because Dr. Marks' opinion is based on a false assumption regarding the onset of J.R.B.'s condition, and the incorrect assumption of a "stepwise regression" after each vaccine administration, it should not be credited.")

These factors prevent petitioner from preponderantly establishing that any logical sequence of cause and effect links her vaccination to her alleged injury based on Dr. Tornatore's opinion. Although parts of this analysis call upon the prior discussion of *Loving* prongs one through three, for the reasons discussed in this section, these same factors prevent petitioner from meeting her burden of proof under either a *Loving* or *Althen* analysis. That is, petitioner has failed to show that she suffered an initial post-vaccination reaction. She has also failed to show in turn that her vaccine thereby *either* significantly aggravated any preexisting microvascular disease *or* acted in concert with her cardiovascular risk factors to cause-in-fact an acute cerebrovascular episode. And, under either approach, she has not preponderantly linked her epilepsy to her cardiovascular health or identified any clear onset of seizures that could place her alleged seizure disorder as occurring post-vaccination.

Of all the treating physicians that cared for petitioner, only Dr. Thomas expressed any opinion that is consistent with Dr. Tornatore's opinion. Specifically, Dr. Thomas took a history from petitioner that included bilateral hand spasms, hallucinations, and memory problems, all arising for the first time post-vaccination in the context of constitutional symptoms such as fever and chills. From that clinical picture, she suggested a hypertensive urgency or stroke as a possible explanation. (Ex. 12, p. 17.) Later, she wrote a letter indicating that petitioner should refrain from future flu vaccines due to a prior severe reaction to flu vaccination. (Ex. 11, p. 1.) However, for all the reasons discussed throughout this decision, Dr. Thomas's opinion necessarily suffers all of the same infirmities as Dr. Tornatore's. And, like Dr. Tornatore, she was not petitioner's treating physician with respect to the initial illness that petitioner has characterized as a vaccine reaction, but which was diagnosed as a viral illness. On the whole, petitioner's treating physicians did not express opinions consistent with either Dr. Tornatore's theory specifically or with vaccine causation of petitioner's condition more generally.

In light of all of the above, petitioner has not met her preponderant burden of proof with respect to *Althen* prong two/*Loving* prong five.

f. *Althen* prong three/*Loving* prong six

The third *Althen* prong/sixth *Loving* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury. *Id.*; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877, at *26 (Fed. Cl. Spec. Mstr. May 30, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Here, Dr. Evans is persuasive on two points that defeat petitioner's claim under *Loving* prong six/*Althen* prong three. First, Dr. Evans is persuasive in explaining that permanent memory loss due to epilepsy requires repeated seizures occurring over an extended period. (Tr. 223-24.) Thus, even accepting *arguendo* that petitioner's memory problems began soon after vaccination and in the context of what is discussed above as a viral illness, this would suggest that her epilepsy and seizure activity, which were otherwise subclinical, would have begun prior to vaccination. Second, in the context of a more minor stroke or cerebral vascular accident of the type that would necessarily be implicated here based on the lack of subsequent MRI evidence, Dr. Evans explains that the onset of epilepsy usually does not occur until months after the initiating event. (Tr. 226.) Here, however, Dr. Tornatore places the onset of seizure

activity contemporaneous to the alleged cerebral vascular accident in the context of petitioner's presentation with constitutional symptoms and memory problems. Even if a three-hour period of onset is potentially consistent with a cytokine response to vaccination, petitioner has not established that the temporal relationship between the allegedly resulting cerebrovascular event and the epilepsy is appropriate.

Thus, petitioner has not met her burden of proof with respect to *Althen* prong three/*Loving* prong six.

VII. Conclusion

Notwithstanding the lack of any definitive diagnosis, there is no question that petitioner suffers a condition that has profoundly affected her life. She has my sympathy and I do not question her sincerity in bringing this claim. However, for all the reasons discussed above, I find that petitioner has not met her burden of proof in this case. Therefore, this case is dismissed.[14]

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master

[14] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.